HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use ERTAPENEM FOR INJECTION safety and effectively. See full prescribing information for ERTAPENEM FOR EDTADENEM for injection, for intravenous or intramuscular use

Initial ILS, Annroval: 2001

INDICATIONS AND USAGE

- Entapenem for Injection is a penem antibiotechial indicated in adult patients and pediatric patients (3 months of age and older) for the treatment of the following moderate to severe infercione caused by supervisible burdness.
- complicated by susceptible bacteria: Complicated intra-abdominal infections (1.1) tions including diabetic foot infections without
- Complicated intra-autominal mechanis. Complicated skin and skin structure infe orteormalitie (1.2)
- 2) ired nosumonia (1.2)

DOSAGE AND ADMINISTRATION
Do not mix or co-induce Extragramm for highering with other medications. Do not use diluments containing destroys (c-0-guesce), 2.1)
Extpensen for highering relatives (c-0-guesce), 2.1)
Extpensen for highering relatives (c-0-guesce), 2.1)

- Prophylactic regimens. (2.1) Doging considerations should be made in adults with advanced or end-stage regal immairment
- hose on hemodialysis. (2.4, 2.5)
- ment regiment: Adults and pediatric patients 13 years of age and older. The dosage should be 1 gram
- Addust and persamp parents (1) years of any and oncer. Ine occupe should be of Partents 3 months to 12 years of any and to the data interface of 15 mg/ls three daily (not to exceed 1 gibby intravenously or intramucularly) (2.2) intravenous intravenously into maly be addinisted on a load and added and addinist for us to 14 days or aphysics regimen for adults: 1 gram angle does given 1 har prior to elective colrectal surgery, (2.3)

- DOSAGE FORMS AND STRENGTHS For injection: Single-dose vial 1 gram. (3)

FULL DRECORDING INFORMATION, CONTENTS

- INDICATIONS AND USAGE ICATIONS AND USAGE Complicated Intra-Abdominal Infections Complicated Skin and Skin Structure Infections, Including Diabetic Foot Infections 12 Complicated Skin and Skin Structure Infections, Including Diabetic Foot Infections
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 14 Community Acquired Pressurements
 15 Acute Preve Department Incompression, Security Control and
 16 Security Preve Department Incompression, Security Control and
 17 Department
 18 Department
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- SAGE AND ADMINISTRATION Instructions for Uke in All Patients Treatment Regimen Prophytactic Regimen in Adults Patients with Renal Impairment Patients on Hemodalyais Patients with Hegalic Impairment Preparation and Reconstitution for Administration
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- CONTRAINDICATIONS
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- 1 INDICATIONS AND USAGE

1.1 Complicated Intra-Abdominal Infections

complicated intra-Abdominal Intections enem for Intection is indicated for the treatment of adult estimate and participic ratiante Ertopeten für injection is inflicated for the treatment or adult patients and peciatific patients (3) months of age and older) with complicated intra-abdominal infections due to Escherichu coli, Chestristum closthidolome, Estandenium lentum, Peptostreptococcus species, Bacteroides Hagilis, Bacteroides distavoris, Bacteroides orativa, Bacteroides Hetaliatomicron, o

1.2 Complicated Skin and Skin Structure Infections, Including Diabetic Foot Infections without Osteonneshine

withing of the operating of the second secon

Builde in obstance from intercontrar wind concentration determinates give cluncar statutes (14); 13. Community Acquired Presumonian Ertaportem for Injection is indicated for the treatment of adult patients and pediatric patients (3) months of age and older) with community acquired penetuminis due to Experisorcana presumonaie (pericalitie susceptible isolates only) inclusing cases with concurrent backerensis, Hammophilas imitatume pedia-traitames negative isolates only, or Marcanie Cardimalian.

1.4 Complicated Urinary Tract Infections Including Pyelonephritis Ertapenem for Injection is indicated for the treatment of adult patients and pediatric catients

3 months of age and older) with complicated unitary tract infections including pyelonephritis due to Escherichia coli, including cases with concurrent bacteremia, or Klebsiella pneumoniae

1.5 Acute Pelvic Infections Including Postpartum Endomyometritis, Sentic Abortion

I Post Surgical Gynecologic Infections m for Injection is indicated for the treatment of adult patients and pediatric catients Competitor for impediate to indicator fue discriminant or back parents are posterior proteiner proteiner (3) months of age and older) with acute pelvic infections indicing postartum endomyometrifis septic abortion and post surgical gynecological infections due to Streptococcus agalacita Escherichia cui, Bacteriorider fragils, Purphyromonase asaccharolytica, Peptosterptococcu

1.6 Prophylaxis of Surgical Site Infection Following Elective Colorectal Surgery Ertapenem for Injection is indicated in adults for the prevention of surgical site following electrice colorectal surgery. y infection

12 Wages consistent of use endoting the state of the s 2 DOSAGE AND ADMINISTRATION

- 2.1 Instructions for Use in All Patients For Intravenous or Intramuscular Use

DO NOT MIX OR CO. INCISE EPTAPENEM EOR IN JECTION WITH OTHER MEDICATIONS. DO

Do not mux on Co-Invises EntraPresen Poin nucleicition with Others medications. So of WISs DULBERS Contaniants Distributions (e.g. -0-200258), which is the second point of the second po

CONTRAINDICATIONS -CONTRAINDICATIONS -CONTRAINDICATIONS -Known hypersensitivity to product components or anaphylactic reactions to β-lactams. (4) Due to the use of lidocaine HCI as a diluent, Entapenem for Injection administered

anesthetics of the amide type (4) -WARNINGS AND PRECAUTIONS -

- Serious humaneansitivity (anapholastic) reactions have been reported in notients receiving Jactame (5.1)
- ures and other central nervous system adverse experiences have been reported an treatment (5.2) eatment. (5.2) nistration of Erlanenem for Injection with valomic acid or divaloper sodium

tailarly is contraindicated in patients with a known hypersensitivity to loca

- duces the serum concentration of valproic acid potentially increasing the risk of m concent reaktivough seizures. (5.3) Zostridioides difficile-associated diarrhea (ranoino from mild diarrhea to fatal colitisi:
- Lossnakodes amche-associated diarmea (ranging from mild diarmea to ratal collos): Evaluate if diarrhea occurs. (5.4) Civilian should be taken when administerion Ertanenem for Injection intramuscularly to
- aunit inatvertent injection into a blood vessel 45.5 ADMEDICE DEACTIONIC

Adults: The most common adverse reactions ($\gtrsim 5\%$) in patients treated with Ertapenem for Injection, most common adverse reactions (c >>) in patients treated with trappetent for injection, using those who were switched to therapy with an oral antimicrobial, were diarrhea, asea, headache and infueed vein complication. (6.1) he prophylaxis indication the overall adverse experience profile was generally comparable hat doserved for ertapenen in other clinical triats. (6.1)

Pediatrics: Adverse reactions in this population were comparable to adults. The most common adverse

reaction (collector) and population which compliance on action in the dominant borrange reactions (c) 5% in pediatric patients treated with Erlapenen for injection, including those who were switched to therapy with an oral actimized and with Erlapenen for injection, including those of the second or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

DRUG INTERACTIONS Co-administration with probenecid inhibits the renal excretion of ertapenem and is

- Co-administration with probeneoid inhibits the renal excretion of ertapenem and is therefere not recommended (7.1). The concomitant use of ertapenem and valproic axid/divalproex solidium is generally not recommended. Arti-laxetimatis other than cartapenemes should be conadered to treat infections in patients whose seizures are well controlled on valproic axid or divalproex solium. (52, 7.2)
- HEE IN CORCURS DODUL ATIONS -----Darol Impoirment: Does adjustment is reco inine clearance is < 30 ml /min/1 72 ml

See 17 for PATIENT COUNSELING INCOMMATION

- DRUG INTERACTION 7.1 Probenecid USE IN SPECIFIC POPULATIONS
 - 8.1 Pregnancy 8.2 Lactation 8.4 Pediatric Use 8.5 Geriatric Use 8.6 Patients with Renal Impairment 8.7 Patients with Hepatic Impairme

10 OVERDOSAGE

- 11 DESCRIPTION 12 CUNICAL PHARMACOLOGY 12.3 Pharmacokinetics 12.4 Microhiology
- NONCLINICAL TOXICOLOGY 13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility 13.2 Animal Toxicology and/or Pharmacology
- 14 CLINICAL STUDIES 14.1 Adults 14.2 Pediatric Patients
- 16 HOW SUPPLIED/STORAGE AND HANDLING
- 16.1 How Supplied
- 17 PATIENT COUNSELING INFORMATION

"Sections or subsections omitted from the full prescribing information are not listed

2.2 Treatment Regimen

- 13 years of age and older The does of Ertapenem for Injection in patients 13 years of age and older is 1 gram (g) given once a dwy (gee Clinical Pharmacology (12.3)).
- 3 months to 12 years of age The dose of Ertapenem for Injection in patients 3 months to 12 years of age is 15 mg/kg twice daily (int) to exceed 1 of tay.
- Tabla 1 presente trastment mideliner for Ertenenem for Injection
- Tuble 1 Treatment Guidelines for Adults and Pediatric Patients With Normal Renal Function* and Body Weight (LV. or LM.) Adults and Daily Dose (I V or I M) Pediatric Patient 13 years of age and older Pediatric Patien 3 months to 12 years of ap Duration of Tota Antimicrobia Infection Complicated intra-abdomina 15 mg/kg wice daily? 5 to 14 days 1 a infections Complicated skin and ski structure infections, including diabetic foot infections¹ 15 mp/kg twice daily? 1 g 7 to 14 days¹ Community serviced 15 mg/kg twice daily 1 a 10 to 14 days Complicated uninary tract infections, including 1.0 15 mg/kg twice daily? 10 to 14 days! nvelonenbritis Acute pelvic infections including postpartum endomyometritis, septic 15 mg/kg twice daily? 1.0 3 to 10 days abortion and post surpical
- due to the designated pathogens [see Indications and Usage (1)]
- not to exceed 1 g/day Estapenem for Injection has not been studied in diabetic foot infections with concomitant
 - ¹ Ertapenen for injection has not been studied in diabetic foot infections with concomiant obscremptific face distincial Studies (7:1-12); ¹ studi patients with diabetic foot infections received up to 28 days of treatment (parenterial or parenterial place on switch therapy). ⁴ daration includes a possible switch to an appropriate oral therapy, after at least 3 days of parenterial place oral, once clinical important has been demonstrated.

2.2 Prophylactic Baniman in Adulte

2.5 Detiants on Homediabusis

2.6 Patients with Henatic Imnairmen

Females

USE DILLIENTS CI

ADMINISTRATION

2 Cor

ADMINISTRATION

Davised: 02/2022

Table 2 presents prophylaxis guidelines for Ertapenem for Injection

Prophylaxis	Guidelines for Adults	

5.2 Cainura Datantial

it should be decreased or decontinued

5.2 Interaction with Valernic Acid

5.5 Caution with Intramuccular Administration

5.6 Development of Drug-Resistant Bacteria

5.7 Laboratory Tests

ADVEDSE DEACTIONS

6.1 Clinical Trials Experience

Arbuarea Evente

Sustamir

Edams/mailing

Abdominal pair

ristipation

Alteced mental status

Hypotension

Diarrhea

Nausea

Vomition

Dizziness

Headache

Dyspnea

ruritus

drug.

Death

Fever

5.2 Sciume Potential Sciume and other central nervous spetem (XIS) adverse experiences have been reported during treatment with Estapenen for injection *face Adverse PacaSong (B, J)*. During dirical intersignation in advit patient bratevie with "Estapenen for lengticon (1 g once adv), seizures, irrespective d'orga relationship, occurred in 0.5% of patients during study therapy plus 14-day follow-up period (<u>BorkAverse PacaDors</u>) (*T)*. These experiences have occurred most commonly

In patients with Los obsorres (e.g., scale essents or history) or secures) and/or componities terral function. Cross adherence to the necommended dusge regiment is surget, sepecially in patients with innon factors that predispose to consulsive activity. Anticonvolution theory should be continued in patients with innon essaire disorders it. Fload terrans, myolocular, or secures occur, patients should be evaluated neurologically, placed on anticonvolution therapy if not aready instituted, and the dosage of Engenemic Integration ne-examined to determine whether

5.3 Interaction with Valprick Add Care report in the Internation have shown that the -advinishtation of carbageneems, helding withprice add concentrations. The values card concentrations may always the start of the end of the start of the start of the start of the start of the the interaction. The origination of endpoints and the carbageneem backwares this interaction. The concentration are of endpoints and the carbageneem backwares and one of the start of the start of the carbageneem backwares and the carbageneem backwares and start of the carbageneem backware and the carbageneem backw

Clostridioides difficile-Associated Diarrhea (CDAD) CDAD has been reported with use of nearly all antibacterial agents, including ertapenem, and

CRAP has been reported with use of nearly all antibiotential agents, including entryeness, nearly non-markers in service from mick planning biologicality, including the service of the s

administration of antibacterial agents. If CDAD is suspected or confirmed, ongoing antibiotic use not directed against *Clostridioides* In Code is suspected on commercial unique and the subscription of the subscription of

Caution should be taken when administering Ertapenem for Injection intramuscularly to avoid inadvertised injection into a blood vessel (see Rosane and Administration /2 7/1

6.9 Development of Drug-Resistant Bacteria with other abilitotics, protopolit user of Ethereten for Injection may result in overgrowth if non-association and the state of the patient's condition as essential. If resolution is the state of the resolution of the state of the resolution of the state of

While Entapement for injection possesses toxicity similar to the beta-lactam group of antibiotic periodic assessment of organ system function, including renal, hepatic, and hematopoletic, advisable during prolonged therapy.

ADVERSE FLEATIONS following are decorted in protein detail in the Warrings and Precasitions section. Hypersimilarity Reactions (see Warrings and Precasitions (5.1)) Interactions with Various Acid and Acid Interactions with Various Acid (see Warrings and Precasitions (5.4)) Caterin with Hinternucature Administration (see Warrings and Precasitions (5.4))

Development of Drug-Resistant Bacteria (see Warnings and Precautions (5.6) Laboratory Tests (see Warnings and Precautions (5.7))

of another drug and may not reflect the rates observed in nractice

Because clinical trials experience Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials

Adults Receiving Entapenem for Injection as a Treatment Regimen Clinical trials enrolled 1954 patients treated with Entapenem for Injection: in some of the clinical

trinic, parenteral therapy was followed by a switch to an appropriate crait antimicrobial (see Chinical Shudies [14]). Most adverse experiences reported in these chinical trials were described as mild to moderable in severity. Ertapenen for Injection was discontinued due to adverse experiences in 4.7% of patients. Table 3 shows the incidence of adverse experiences reported

patients treated with Ertapenen for injection, including troop who were switched to therapy with an oral antimicrobial, were diarrhea (5.5%), infused vein complication (3.7%), nauses (3.1%), headache (2.2%), and vaginitis in females (2.1%).

Table 3

Tazobactam 3.375 g q6h

79 5.4 67

66

1.4

5.4 33

2.6

Includes Phase Ib/II Complicated intra-abdominal infections. Complicated skin and skin

Includer solitation, confusion, discrimination, decreased mental acuity, channed mental status

In patients treated for complicated intra-abdominal infections, death occurred in 4.7% (15/316) of patients receiving Ertapenem for Injection and 2.6% (8/307) of patients receiving comparator

In clinical trials, seizure was reported during study therapy plus 14-day follow-up period in 0.5% of patients treated with Ertapenen for Injection, 0.3% of patients treated with piperacillin/ tazabackam and 0% of patients treated with celfixozone (see Marxings and Precaviors (5.2)).

Additional adverse experiences that were reported with Ertapenem for Injection with an incidence > 0.1% within each body system are listed below

Body as a Whole: abdominal distention, pain, chilis, septicernia, septic shock, dehydration, gout, makibe, asthenia/latigue, necrosis, candidiasis, weight loss, facial edema, injection site induration, injection site pain, extravasation, philebitis/thromophilebitis, fank pain, sprincope

les Phase IIb/II Community acquired pneumonia and Complicated uninary tract infections

These deaths occurred in patients with significant co-morbidity and/or severe baseline ions. Deaths were considered unrelated to study drugs by investigators.

1 g daily or 2 g dail

2.0

1.5 2.1

23 1.5

3.4

.

2.5

24

1.9

ence (%) of Adverse Experiences Reported During Study Therapy Plus 14-Day Follow-Up in > 2% of Adult Patients Treated With Ertapenem for Injection in Clinical Trials

references in 4.74 or patients, rate 3 shows the inductive or adverse experience $\geq 2\%$ of patients in these trials. The most common drug-related adverse exp isents treated with Ertapenem for injection, including those who were switched

Entanement for Pineracillin/

2.5 16 13 1.6

3.6 4.8 4.3 3.9

10.2 12.1 0.2

85 87 64 7.4

51 34

5.6 54 6.8 6.9

26 1.8

2.5

structure infections and Acute pelvic infections trials

in patients with CNS disorders (e.g., brain lesions or history of seizures) and/or com

Cardiovascular System: heart failure, hematoma, chest pain, hypertension, tachycardia,

cardiac arrest, bradycardia, anhythmia, atrial fibrillation, heart murmur, ventricular tachycardia, axystole, subtural hemoritane

asysobe, subulari inninninge Digestive System: acid regurgitation, oral candidasis, dyspepsia, gastrointestinal hemorrhoge, anorexia, liatulence, C. divilical-essociable diarrhea, stomatilis, dysphagia, hemorrhoids, lieus, choleitithiasis, duodenitis, esophagitis, gastritis, jaundice, mouth ulcer, pancreatitis, pyloric

Nervous System & Psychiatric: anxiety, nervousness, seizure (see Warnings and Precautions (5.21) formor decreasing hyperblasia spage parethesia approxime behavior writing

(a.c.y), enitor, opresaint, nypesaintsa, spasin, pareamesa, aggressire ontarium, verugo Respiratory System: cough, pharyngtis, rales/rhonchi, respiratory distress, pleural effusion, hypoxemia, Evonchoconstruction, pharyngeal discomfort, epistaxos, pleuritic pain, asthma, hemotypisis, hiccups, voice disturbance

Skin & Skin Appendage: erythema, sweating, dermatitis, desquamation, flushing, urticaria

Bronanital Surfam ranal immainment oficuria/anuria vaninal nouribur hamsburia urinan

Urogental System: renal impairment, orgunaranuna, vaginal pruntus, nemanuna, urmary retention, bladder dysfunction, vaginal candidiasis, vulvovaginitis. In a clinical trial for the treatment of diabetic foot infections in which 289 adult diabetic patients

are trasted with Erbanenem for Injection. the scheres eventiance confile user generally similar

to that seen in previous district trutts. Provintissus of suggests 20 km infection following Elective Colorestal Suggery both suggests and the second second second second second second second second colorestal supery in which 4/2 patientit received a 1 g does of Erlapsenem for itselform 1 may not be suggery and when the followed is a table 1 d days port supery, the overall adverse supervised patients and patients and the second second second second second periodic days and the second second second second second second second periodic days and the second second second second second second second second periodic days and the second second second second second second second second periodic days and a second second second second second second second second second periodic days and the second secon

Incidence (%) of Adverse Experiences Reported During Study Therapy Plus 14-Day Follow-Up in > 2% of Adult Patients Treated With Estapenem for Injection for Prophytaxis of Surgical Stel Infections Following Petrolew Collegency of Surgical

N = 476

21

2.3

2.0

65

20

34

Additional adverse experiences that were reported in this prophylaxis trial with Ertapenem for Injection, regardless of causality, with an incidence > 0.5% within each body system are listed and the statement of the system and the system and the system are listed as a system as a system and the system are listed as a system and the system are listed as a system as a system are listed as a system and the system are listed as a system as a system are listed as a system Exercipterinal Dirorders: C difficiliainfaction or colitie dos mouth hamstochasis

Injury, Poisoning and Procedural Complications: incision site complication, incision site

Respiratory, Thoracic and Mediastinal Disorders: crackles lung, lung infiltration, pulmonary

congestion, puintovary emocisim, winecarq. Pediatics Estimets Receiving Estaparement for injection as a Tirstatment Regimen Clinical tristie enrolled 384 patients treabed with Estapenent for injection; in some of the clinica Tirstic, parentieral Tirstieray was followed by a switch to an appropriate cara alminicrobial (see Clinical Studies (74)). The orwaral adverse experience profile in pediatric patients in some of to fault in solution priorities. Table 5 shows the incidence on daverse experiences reported in >27.

to initial abun patients, rate of sources in including data and the experimental experiments in patients in clinical trains. The most common drug-related adverse experiments in pediatric patients treated with Ertagenern for Injection, including those who were switched to therary with an oral antimicrobial, were datametera (6.5%), infusion site cash (5.5%). Infusion site

Table 5 Incidence (%) of Adverse Experiences Reported During Study Therapy Plus 14-Day Follow-Up in ≥ 2% of Pediatric Patients Treated With Ertapenem for Injection in Clinical Trials

3

tinal stoma complication anastomotic leak secona wound debiscence

Infections and Infestations: cellulitis, abdominal abscess, fungal rash, pelvic abscess

General Disorders and Administration Site Condition: crepitations

Musculoskeletal and Connective Tissue Disorders: muscle spasms

3.9

47

2.3

10.2

4.9

2.3

....

4.4

4.7

29

cidence > 0.5% within each body system are listed belo

Matabalism and Natrition Disorders: decreased annality

Rennductive System and Breast Disorders: cenital rash

Nervous System Disorders: dizziness, somnolence

Musculoskeletal and Connective Tissue Disorders: arthraicia

Gastrointestinal Disorders: nausea

Psychiatric Disorders: insomnia

Vascular Disorders: phlebitis

"Include Russes Boungicated data not data that uncluse infections. Community acquired promotions can compare and unreal and infections that in the incluse that in the that the second s

Additional adverse experiences that were reported with Ertanenem for Injection with an

General Disorders and Administration Site Condition: hypothermia, chest pain, uppe addominal pain; infusion site pruntus, induration, philebitis, swelling, and warmth

Infections and Infestations: candidiasis, oral candidiasis, viral pharyngitis, herpes simplex var infection, abdominal abozess

Respiratory, Thoracic and Mediastinal Disorders: wheezing, nasopharyngitis, pleural effusion, rhnritis, rhinomhea Skin and Subcutaneous Tissue Disorders: dermatitis, pruritus, rash erythematous, skin lesion

Nervous System Disorders: cerebrovascular accident

Renal and Urinary Disorders - dururia pollakiuria

cestion, pulmonary embolism when

ms (2 E%) somiting (2 1%)

Adverse Event

Infusion Site Frythem

Infusion Site Pair

Abdominal Pair

Constination

Looze Stoole

Unper Respiratory Tract

Diaper Dermatitis

Vomiting

Headache

Counth

Rash

Doraria

Local:

Systemic

2 g

1.0

6.6

124

1.9

Clavulan... (N=24)

83

20.8

42

4.2

0

83

8.2

83

E50000400519

tennsis

Mucculaskeletal System: len roin

Special Senses: taste perversion

suggith in > 2% of nationale in this trial

Adverse Events

-

Protonarotioa infactio

University teact infaction

Wound complication

Wound infection

Melectaria

Small intertinal obstruction

Indication	Daily Dose (I.V.) Adults	Recommended Duration of Total Antimicrobial Treatment
Prophylaxis of surgical site infection following elective colorectal surgery	1 g	Single intravenous dose given 1 hour prior to surgical incision
.4 Patients with Renal Impairm rtapenem for Injection may be used	ient i for the treatment of i	infections in adult patients with rena

traplement for injection may be used to be detailed of information in action to appendix with relation impairment. In patients whose creatinine clearance is > 00 mL/min1/7.3 m², no dosage adjustment is necessary. Adult patients with severe renal impairment (creatinine clearance < 30 mL/min1/7.3 m²) and creatine clearance < 10 mL/min1/7.3 m².

2.3 Patients on Hemodiayias are given the econometod daily located 500 mg of thems addit galatiest on hemodiayias are given the econometod daily located 510 mg to the econometod location of 110 mg to econometod locations the hemodiayias areas and the econometod locations are been at location of the econometod locations are been at location and the econometod location are been at location and the econometod location of the econometod location are been at location and the econometod location are been at location are been at location and the econometod location are been at location are been at location and the econometod location are been at location are been

¹Cockcroft and Gault equation: Cockcroft DW, Gault MH. Prediction of creatinine clearance from serum creatinine. Neptron. 1976

2.6 Patients with Hepatic Impairment No dose adjustment recommendations can be made in patients with hepatic impairment (see Use in Specific Productions (8.7) and Christal Pharmacology (12.3).

Preparation for intravenous administration: no wort way no coultering partnership in rection with other menucations: no not

ERTAPENEM FOR INJECTION MUST BE RECONSTITUTED AND THEN DILUTED PRIOR TO

Preparation for inframuscular administration: ERTAPPINE MPG IN INJECTION MUST BE RECONSTITUTED PRIOR TO ADMINISTRATION. 1. Reconstitute the contents of a 1 g vai of Estapenem for lipecian with 3.2 m. d 1 % libocate IPC lipeciator¹ (whitout epinophrine). Shoke viai throatophy to form solution. 2. Immediately withfram the contents of the viai and administer by deep inframuscular injection in a large market mask (such as the gluteel musted or labera) and the

thigh). The reconstituted I.M. solution should be used within 1 hour after preparation.

NOTE: THE RECONSTITUTED SOLUTION SHOULD NOT BE ADMINISTERED INTRAVENOUSLY

Preparation for intravenous administration: DO NOT MIX OR CO-INFUSE ERTAPENEM FOR INJECTION WITH OTHER MEDICATIONS. DO NOT

FRIAPENEM FOR INJECTION MUST BE RECONSTITUTED AND THEN DILUTED PRIOR TO

STRATION. Reconstitute the contents of a 1 g vial of Ertaportem for hijection with 10 mL of one of the following Water for hijection, 0.9% Sodum Chontee hijection or Baterioratatic Water for hijection, using a synipte equipative thin a 2-1 gapate or mailer id ameter needle. MOTE: Use with a needleties W system is not recommended. State well to discoste and immediately withintara avalume equipation of 5 mg/aq d body weight not be screed 1 gibly and diate in 0.9% Sodum Chontee hijection of Engeneme concentration of 2 symptm. Or sec. Discassi with this made potion of Engeneme

Reconstitute the contents of a 1 g vial of Ertapenern for Injection with 3.2 mL o 1% lidocaine HCI injection? (without epinephrine). Shake vial thoroughly to form

solution. immediately withdraw a volume equal to 15 mg/kg of body weight not to exceed 1 g/dsg/ and administer by deep inframacoular injection into a large muscle mass (auchr as the g/utell muscles or talenel part of the thing). Discard value with unused portion of Estapement for injection reconstituted solution. The reconstituted I.M. solution should be used within 1 hour after preparation.

NOTE: THE RECONSTITUTED SOLUTION SHOULD NOT BE ADMINISTERED INTRAVENOUSLY.

Storage When prepared with the diluent Erlanenem for injection maintains satisfactory potency for

snoution not be trozen. Befere administering, see accompanying package circular for Ertapenem for Injection. Parenteral drug products should be inspected visually for particulate matter and discoloration prior to use, whenever solution and containter permit. Solutions of Ertapenem for Injection range from colorises to pade velow. Visitions of color within the range do not affect the potency o

Estapenem for Injection is a sterile lumbilized number in a single-dose vial containing 1 m m sodium for intraven

CONTRAINDICATIONS Fritagenem for Injection is contraindicated in patients with known hypersensitivity to any

CONTRANSICIATIONS Extrement for injection and or individual patients with survent hypersensitivity to any effection and or individual and or individual and an extreme the set of the patients who have demonstrated anaphylactic reactions to beth-statums. Due to the use of idiocate HC as a clikent, Extrement for lejection administered intramuscularly is containdicated in patients with a known hypersensitivity to local amerithesis of the anide type.

us and occasionally fatal hypersensitivity (anaphylactic) reactions have been reported

in patients receiving therapy with behavior patients are more likely to occur in individuals with a history of sensitivity to multiple allergers. There have been report of individuals with a history of sensitivity to multiple allergers. There have experienced sever

sensitivity reactions when treated with another beta-lactam. Before initiating the mem for Injection, careful inquiry should be made concerning previous hypers

reactions to enclose replacing to the intervent of the induction of the in

mmu prepared with the druent, Ertapenem for Injection maintains satisfactory p 6 hours at room temperature (25°C) or for 24 hours under refrigeration (5°C) within 4 hours after removal from refrigeration. Solutions of Ertapenem for should not be frozen.

Reconstitute the conduction of a 1 yeal of Estaporem for hipsciton with 10 nr. of one of the following Water for hipsciton, 0 years a single space of the single space of the single space of the space Reconstitute the contents of a 1 g vial of Ertapenem for Injection with 10 mL of one

(weight in kg) x (140-age in years)

(72) x serum creatinine (mg/100 ml

(0.95) v (volue calculated for maler)

27 Preparation and Reconstitution for Administration

Adults and pediatric patients 13 years of age and older

Dranspotion for intramunoutar administration-

efer to the nesscribing information for Educaine HC

Injection reconstituted solution. Complete the infusion within 6 hours of reconstitution.

ERTAPENEM FOR INJECTION MUST BE RECONSTITUTED PRIOR TO ADMINISTRATION.

Pediatric patients 3 months to 12 years of age

Presention for intramuscular administration

Refer to the nescribing information for lidocaine HCI

3 DOSAGE FORMS AND STRENGTHS

penem equivalent to 1.046 g ertape tion after reconstitution.

WARNINGS AND RECAUTIONS

5.1 Hypersensitivity Reactions

solution

the product

For Injection: Vials

upplementary dose of 150 mg is recommended if entapenen is administered within 6 hours prio secondarias in the second sec

6.2 Port-Marketing Experience

6.2 Post-Marketing Experience The following additional adverse reactions have been identified during the post-approval use of Ertapenem for Injection. Because these reactions are reported voluntarily from a population of uncertain size, it is not adverse possible to reliably estimate their frequency or establish a causal relationship to drup exposure

Gastrointestinal Disorders: teeth staining

Immune System Disorders: anaphylaxis including anaphylactoid reactions Muscularkalatal and Connective Tireus Disorders: muscular weekness

Nervous System Disorders: coordination abnormal, depressed level of consciousness, divisionesia, oait disturbance, myocionus, tremor, encenhalocathy (recovery was protonged in estiante with ranal immorrhante.

Psychiatric Disorders: altered mental status (including appression, delinium), hallucinations Skin and Suboutaneous Tissue Disorders: Acute Generalized Exanthematous Pustulosis (AGEP). Drug Reaction with Epsinophila and Systemic Symptoms (DRESS syndrome). vpersensitivity vasculitis

Adverse Laboratory Changes in Clinical Trials

6.3. Adverse Laboratory Changes in Citical Triats Adults Reverse (Tarternitor Interpretation attriated Realing Laboratory adverse experiences that were reported damp therapy in 2 2% of adult patients beated with Flappenets to Implement in Citical active presented in Table 45. Dray-related treated with Flappenets to Implement and Table active presented in Table 45. Dray-related treated with Flappenets for lightCitical Citical City and Citical City and Citical Interpretation of the Interpretation of Citical City and Citical City and Citical Interpretation of the Interpretation of Citical City and City and City and City and Interpretation of City and City and City and City and City and City and Interpretation of City and City and City and City and City and City and and citorofistual data to Interpretation City and City and City and City and and city and City and Databatic City and City and City and City and and city and City and Databatic City and City and City and City and and city and and City and City and Databatic City and City and City and City and and City and and City and and City and and City and and City and and City and City and City and City and City and City and and City and and City and and City and and City and and City and and City and and City and and City and City and City and City and Ci

Table 6

Table 6 Incidence* (%) of Laboratory Adverse Experiences Reported Durin Day Follow-Up in > 2% of Adult Patients Treated With Ertapenem fo ces Reported During Study Therapy Plus

Adverse Laboratory experience	Ertapenem for Injection ² 1 g daily (n ² =766)	Piperacillin/ Tazobactam ² 3.375 g q6h (n ¹ =755)	Ertapenem for Injection ¹ 1 g daily (n ¹ =1122)	Ceftriaxone ¹ 1 or 2 g daily (n ¹ =920)
ALT increased	8.8	7.3	8.3	6.9
AST increased	8.4	8.3	7.1	6.5
Serum alkaline phosphatase increased	6.6	7.2	4.3	2.8
Eosinophils increased	1.1	1.1	2.1	1.8
Hematocrit decreased	3	2.9	3.4	2.4
Hemoglobin decreased	4.9	4.7	4.5	3.5
Platelet count increased	6.5	6.3	4.3	3.5
Urine RBCs increased	2.5	2.9	1.1	1
Irina WBCe increased	2.5	2.2	16	11

Number of patients with laboratory adverse experiences/Number of patients with the

Isocratry test. Number of patients with one or more laboratory tests. Findustes Phase IIb/III Complicated intra-shdominal infections, Complicated skin and skin structure infections IIb/III Complicated intercione trials Includes Phase IIb/III Community acquired phenemonia and Complicated uninary tract infections, and Phase Ita trials

Additional laboratory adverse experiences that were reported during therapy in > 0.1% of patients treated with Ertapanem for Injection in clinical trials include: increases in serum creatinine, esema jucces, BUR, black (inclet and indirect serum birkinha, serum sodium and potassium, PT and PTT; decreases in serum potassium, serum ablumie, WBC, platelet count, and segmented neturphilits.

In a clinical trial for the treatment of diabetic foot infections in which 289 adult diabetic pat were treated with Ertapenem for Injection, the laboratory adverse experience profile erally similar to that seen in previous clinical trials.

Prophylaxis of Surgical Site Infection following Elective Colorectal Surgery

In a clinical trial in adults for the prophysixis of surgical site infection following elective colorectal surgery in which 476 gatients received a 1 g doze of Ertapenem for injection 1 hour prior to surgery and were then followed for safety 14 days post surgery; the overall laboratory adverse experience profile was generally comparable to that observed for Ertapenem for Injection in received.

Pediatric Patients Receiving Ertagenem for Injection as a Treatment Regimen

Cessantic - calentis incontrius Linguentini for injection las a informatin industri Liberatory adverses operationes that were reported during heapy in 2.5% of podiatric patients treated with Entrapenens for injection in clinical triads are presented in Table 7. Drug-related treated with Entrapenens for injection, including those with over entrithed to Braney with an oral antimicrobial, in clinical triads were neutrophil count decreased (5%), ALT increased (2.2%), and AST increased (2.1%).

Table 7 Table 7 Incidence* (%) of Specific Laboratory Adverse Experiences Reported During Study Therapy Plus 14-Day Follow-Up in > 2% of Pediatric Patients Treated With Estapenem for Inj Contract Treated Study St

Adverse laboratory experiences	Ertapenem for Injection (n*=379)	Ceftriaxone (n ^z =97)	Ticarcillin/Clavulanate (n*=24)
ALT Increased	3.8	1.1	4.3
AST Increased	3.8	1.1	4.3
Neutrophil Count Decreased	5.8	3.1	0

Number of patients with laboratory adverse experiences/Number of patients with the laboratory test: where at least 300 patients had the test	
Number of patients with one or more laboratory tests	

Additional laboratory adverse experiences that were reported during therapy in > 0.5% of patients treated with Ertapenem for Injection in clinical trials include: silvaline phosphatase increased, eosimphil count increased, platelet count increased, while blood cell count decreased and urine notein present.

7 DRUG INTERACTIONS

7.1 Probenecid Probenecid interferes with the active tubular secretion of estapenem, resulting in increased pissma concentrations of estapenem (see Clinical Pharmacology (12.3)). Co-administration of probenecid with estapenem is not recommended.

7.2 Valproic Acid

7.2 Subjeck Add Cose reports in the Birstnere have shown that co-administration of carbapenems, including entiperem, to patients receiving regionic add or diviginee subium results in a reduction of values card concentration. The subject card concentration mus any doublewish the frequencies. Although the mechanism of thes interaction is subrown, data from in who and animal studies support that comparements may initial the hybridges of values cardinal studies (Weing and Postantion (2.3).

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary Available data from a small number of postmarketing cases with Ertapenem for Injection Available disk tien a small number of postmaneteling cases with trajeventin the injection and in programs or a small number of postmaneteling cases with trajeventin the inger that disk initiative cases administration of entraneous disk of the intervention of the intervention revisions of other postman and training the provid of organopenesis, here was no evidence of other postman and postmanet at the maximum recommended human does approximately 1.2 limits the human exposure at the maximum recommended human does are comparison. In organism the intervention of the other shares and lacetation, feels taxing, device the starter shares of the approximation of the other in the penetation of the prior adjustment exposure (3.0) organism (3.1). Each human maximum lacetation, feels taxing, device posterial (3.0) organism (3.1). Each human exposure (3.0), organism (3.1). Each prevention of the prior adjustment exposure (3.0), organism (3.1). Each human maximum lacetation, feels taxing, device posterial (3.0), organism (3.1). Each human maximum lacetation (4.0) or the posterial device, and impart exposure (3.1). Cases the human exposure lacetation (4.0) or the human maximum (3.0) organism (3.1). There is the human exposure lacetation (4.0) or the human (3.0) or the human exposure (3.0). Cases the human exposure (3.0), or the human exposure lacetation (4.0) or the human (3.0) or the human exposure (3.0). Or the human exposure (3.0), or the human exposure lacetation (4.0) or the human exposure (3.0). Second (3.0), the human exposure (3.0), the human exposure (3.0), or th at the MRHD (see Data)

at the MRHD (per Data). The estimated background risk of major birth detects and miscarriage for the indicated population is unknown. All programmers have a background risk of birth detect, loss, or other adverse outcomes. In the U.S. general population, the estimated background risk of major birth detects and miscarriage in clinically recognized pregnancies is 2 to 4% and 15 to 20%, respectively.

daily deeper in healthy adulte

	Table 9.	
ration of ertapenem dosages of up to 700 mg/kg/day ed on AUC) during the period of organogenesis (gestation		
r embrurdatal affacte		Plasma Concentration

(approximately 1.2 times the News) case days (GD) 6-20) revealed no maternal or days (ILII) 6-20) revealed no maternal or entryvletial effects. Program mice intravenously, administered ertapearem dosages of up to 700 mg/kg/day (approximately 3 times the MRPID based on body surface area companison) during the period of organogenesis (ISD 6-15) showed slight decreases in average fetal weight and an associated decrease in the average number of ossified sacrocaudal vertebras. There were no maternal

decrease in the average number of ossified successful verticine. There were no maternai effects at any docage. In a pre-postnatal study in rats, entapenem administered to pregnant rats at docages up to 700 migkigity propromitely 1 z. Times the MRHD based on AUC) during organogenesis through lactation, (BD 6 until Lactation Day (LD) 20) did not result in felsi basicly, developmental defines, or impaired reproduction in first generation offspring and feld deaths and malformations were not increased in second generation offspring.

8.2 Instation Risk Summary

Data Animol Data

In pregnant rats, intravenous administ

BirkSummary Entragenem is present in human milk (see Data). There are no data on the effects on the breastled infant or the effects on milk production. The developmental and health benefits of breastleding stould be considered along with the mother's clinical need for Ertapenem for injection and any potential adveces effects on the breastled infant from Ertapenem tor lefection from the underlying maternal condition Data

Data The concentration of ertugement in breast milk from 5 lastating women with pelvic infections (§ b 14 diap) potentially instances of a random time point diap) for 8 contenciation data the concentration of entry of the second s

 8.4 Pediatric Use
 Selety and effectiveness of Ertapenem for Injection in pediatric patients 3 months to 17 years of
 Selety and effectiveness of Ertapenem for Injection in pediatric patients 3 months to 17 years of sately and electroteness of chapterin for improve improvements a matrix of 17 years or age are supported by evidence from adequate and well-controlled trists in adults, pharmacokinetic data in pediatric patients, and additional data from comparator-controlled trials in pediatric patients 3 months to 17 years of age [age Indications and Usage (1-1), (1-2), (1-3), (1-4) and (1-5) and Chirad Shaves (1-4-2).

Ertapenem for Injection is not recommended in infants under 3 months of age as no data are available.

Ertapenem for Injection is not recommended in the treatment of meningitis in the pediatric population due to lack of sufficient CSF penetration. 9.5 Geristric Ilea

It is bename use If the 1.835 patients in Phase 2b/3 trials treated with Ertapenem for Injection.

or an 1,000 percent were 65 and over, while approximately 12 percent were 75 and over. No overall differences in safety or effectiveness were observed between these patients and vourse attients. Other reported clinical expressions has not identified differences in responses between the elderly and younger patients, but greater sensitivity of some olde individuals cannot be ruled out. This drug is known to be substantially excreted by the kidney, and the risk of toxic react this drug may be greater in patients with impaired renal function. Because elderly patient

more likely to have decreased renal function, care should be taken in dose selection, and it may be useful to monitor renal function (see Dosage and Administration (2.2)) 8.6 Patients with Renal Impairment

Dosage adjustment is necessary in patients with creatinine clearance 30 mL/min or less (see Dosage and Administration (2.4) and Clinical Pharmacology (12.3)).

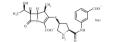
Design and Administration (2.4) and Chancel Hummarology (17.3). **6.7** Testletest with Registic Impairment The glammacolinetics of entryenom in patients with heapdic impairment have not been 19 daily and 30 patients recorring comparate drugs were considered to have Coliki-Hugh Class, A, B, or C loss impairment. The incidence of adverse experimenci in spatient with heaplic impairment was similar between the entryening rouge and the comparator groups.

10 OVERDOSAGE

No specific information is available on the treatment of overdosage with Ertagenem for Injection Intentional overdosing of Ertapenem for Injection is unlikely. Intravenous administration o Ertapenem for Injection at a dose of 2 g over 30 min or 3 g over 1 to 2h in healthy adu perior in injection at a base of growth of any of a growth of a growth of a second sec asse or 40 mg/kg up to a maximum of 2 g cin not result in toxocry. In the event of an overdose, Ertapenem for Injection should be discontinued and general supportive treatment of your until renal elimination bikes bace.

opport to classific or can be removed by hermodalysis; the plasma clearance of the total raction of ertapenem was increased 30% in subjects with end-stage renal clearance when remodalysis (4 hour secsion) was performed immediately following administration. However, or information is available on the use of hermodalysis to treat overcoscape.

11 DESCRIPTION Ertaxenem for Intection is a sterile, synthetic, parenteral, 1-β methyl-carbapenem that is structurally related to beta-factam antibiotics. Chemically, Ertapenem for Injection is described as (48-13(35";55").40;58:68(8"))-3-115-Literacialy, istrapenent or injection is described as (4A+(3,5X),5X),AC26(3,6(7,7)),5-3 [(3-carboxyberr(jamino)carbox/j-3-pyrrolidiny(1)hti)-6-(1-hydroxyethyl)-4-methyl-7-coo-1-azabicyclo [3.2.0]hept-2-ene-2-carboxylic axid monosodium salt. Its molecular weight is 497.5. The empirical formulas is C H N 0.5Ms, and its structural formulas is:



Entanement socium is a white to off-white hyproscopic, weakly crystalline nowder. It is soluble my ster and 0.9% sodium chloride solution, practically insoluble in ethanol, and insoluble in isopropyl acetate and tetrahydrofuran.

Establement for Injection is supplied as shelle lumbilized powder for intravenous infusion after Exaptrent na rejection is support as senire repaintera power na manerada includina and reconstitution unit appropriate laborar (see Dacage and Administration (22)) and transite fo 30 mil. 0.9% Sodium Cherke historica for intramuscular injection following reconstitution with 1% lidocaine hydrochloride. Each single-dose vial contains 1 gram entapenem equivalent to 1.046 grams entapenem sodium. The sodium contert is approximately 132 mg (approximately 6 mG).

Each vial of Ertapenem for Injection contains the following inactive ingredients: 175 mg sodium

12 CUNICAL PHARMACOLOGY

12.1 Mechanism of Action

em sodium is a carbanenem antibiotic. (see Clinical Pharmacology (12.4))

12.3 Pharmacokinetics 13.3 Pharmacokinetics Average plasma concentrations (mcg /mL) of ertapenem following a single 30-minute infusior of a 1 g intravencus (UV) dose and administration of a single 1 g inframuscular (LML) dose in healthy young adults are presented in Table 8.

Table 8 Table 8 Disease Consententions of Education in Adulto Aller Single Deep Administration

Average Plasma Concentrations (mcg/mL)									
Dose/Route	0.5 hr	1 hr	2 hr	4 hr	6 hr	8 hr	12 hr	18 hr	24 hr
1 g LV."	155	115	83	48	31	20	9	3	1
1 g LML	33	53	67	57	40	27	13	4	2

The area under the plasma concentration-time curve (AUC) of edapenem in adults increased dose range, whereas u-dose range, whereas uthere we patient additional transmission in the curve (word) or evapore in additional transmission in the second structure of the transmission of the second structure of the concentration-dependent plasma protein binding at the proposed therapeutic dose (see Clinica Pharmacology (12.3)). There is no accumulation of ertapenem following multiple LV or LM.1 g ons (mco/mL) of ertapenem in pediatric patients are presented in

Table 0 Tai 9 In Dedictric Dationto Alle

Complicated Urinary Tract Infections Including Pyeloneohritis

ical Infections

14.2 Padiatric Patiente

Ertapenem was evaluated in adults for the treatment of complicated urinary tract infectione including ovelonephritis in two randomized, double-blind, non-inferiority clinical trials. Both

inducing systemsprints in two randomized, double-bind, non-interiority clinical triats. Both triats compared enterprint () generating/once ad giv) into clinicano () generatinary once ad giv) into clinicano () generatinary once ad giv) into clinicano () generatinary once ad giv) and enrolled a batal of 800 patients. Both regiments allowed the option to awitch to only clinical systems and the state of the

Acute Pelvic Infections Including Endomyometritis, Septic Abortion and Post-Surgical Symecological Infections

sumacouplan introducts Entrepenen was evaluated in adults for the treatment of acute pelvic infections in a randomized, double-blind, non-inferiority clinical trial. This trial compared entapenem (1 g intravenously once a day) with piperacilin functionatarian (3.375 g intravenously every 6 hours) for 3 is 10 days and errolled 412 cadelets including 302 obtienes with bobter/including and the size and 45 cadelets with section 412 cadelets including 302 obtienes with bobter/including and the size and 45 cadelets with section and a size of the size o

(test-of-cure) were 93.9% (153/163) for ertapenem and 91.5% (140/153) for piperacillin/tazobactan

Distribution of description of the inference for the mean fiber of the description of th

the assessment or that outcome is samples or controlling tactors included plan or concontant antibiotic violators, the need for a second surgical procedure during the study period, and identification of a distant site infection with concornitant antibiotic administration and no evidence of subsequent wound infection. Three-bunched forth-site (Additionation constrained to extension

and assesses in severe influence. These bases of the probability of t

Ertapenem was evaluated in pediatric patients 3 months to 17 years of age in two randomized multicenter clinical trials.

millionizer ordenizat taka. We have a patient for the second s

86. % (2720) the orthanone. The second tail energies the product of the second tail energies the product of the second tail energies the second t

Trace now supplied as a sterile lyophilized powder in single-dose vials containing ertapenem for infravenous infusion or for intramuscular injection as follows:

reconstructors and intervaluation sources The reconstituted solution, immediately diluted in 0.9% Sodium Chloride hijection (see Dosage and Administration (2.7)), may be stored at room temperature (25°C) and used within 6 hours or stored for 24 hours under refrigeration (3°C) and used within 4 hours after removal from refrigeration. Solutions of Enzyperatine for hijection studied not be forcen.

Patients should be advised that allergic reactions, including serious allergic reactions could occur and that serious reactions may require immediate treatment. Advice patients to report any previous hypersensitivity reactions to Ertopenem for Injection, other beta-factams or other allergens.

Patients should be counseled to inform their physician if they are taking valproic acid o

uncome anomative commenses us interm merer preparion in they are taking valgorio: acid or indicatories acidum. Valgorio: acid concentrations in the blood may drop below the therapeutic range upon co-administration with Ertapenen for hijection. If treatment with Ertapenen for injection is necessary and continued, alternative or supplemental anti-convulsant medication to prevent and/or treat seizures may be needed.

to prevent and/or treat sciturers may be netedd. Patterist should becomes that antibateriarial drugs including Entrapenen for hijection atoudd only be used beat bachetia infections. They do not freat viral infections (e.g., the common odd), these Entrapenent for higherion is prevented be beat a bachetin labelera, hashets badout descriptions and the state of the state bachetin labelera. The state back and the state of the state of the state back and the state back and the state back and the state of the state scatter and the state of the state back and the state state and the state of the state state of the state state of the state back and the state state of the state may (1) decrease the followings and its link to be stateble by its fragments for legislations of the antibacket data state in the future.

Diarrhea is a common problem caused by antibiotics which usually ends when the antibiotic is

Datribes it is a common proceen caused by anticonce writin usually enus when ure answ discentinued. Sometimes after starting treatment with antibiotics, patients can develop w and bloody stools (with or without stoarsch cramps and fever) even as late as two or months after having taken the last dose of the antibiotic. If this occurs, patients should or

NDC 63323-823-20 1 gram per vial

Strength

Fach

E50000400519

16 HOW SUPPLIED/STORAGE AND HANDLING

Heit of 10

Do not store lyophilized powder above 25°C (77°F).

Product Code Unit of Sale

Reconstituted and infusion solutions

17.1 Instructions for Patients

17 PATIENT COUNCELING INCORMATION

cian as soon as possible

Manufactured for

Made in Ital.

451641D

Lake Zurich, IL 60047

16.1 How Supplied

16.2 Storage and Handling

Before reconstitution

823120

nical infac

whether The clinical currant rate in the clinically exclusive and via particle and

Prophylaxis of Surgical Site Infections Following Elective Colorectal Surgery

<u>Resistance</u> Ertapenen is stable against hydrolysis by a variety of beta-lactamases, including penicillinases, and cephaloporinases and extended spectrum beta-lactamases. Ertapenem is hydrolyzed by metallo-beta-lactamases.

both in vitro and in clinical infactions so described in the INDICATIONS AND USACE parties

Preventia draw The following in with data are available, <u>but their clinical significance is unknown</u> AI least 90% of the following bacterie exhibit an in with minimum inhibitory concentration (MC) leas than ce equal to be associable tracking of the otherwise. The efficacy of etagenem in testing diriscal infections due to these bacteria has not been established in adequate and web-controlled dirical thuis:

For specific information regarding susceptibility test interpretive criteria and associated test method and quality control standards recognized by FDA for this drug, please see: https://www.fda.gov/STIC

No long-term studies in animals have been performed to evaluate the carcinogenic potential

In chaptenini, Ertapenem was not genotoxic in in vitro or in vivo assays, including: an alkaline elution/ra hepatoxyte assay, a chromosomal aberration assay in Chinese hamster orary cells, a TW human lymphoblastoid cell mutagenesis assay and a mouse microrudeus assay.

In rats, intravenous dosages up to 700 mg/kg/day (approximately 1.2 times the human exposure at the recommended human dose of 1 g based on plasma AUC) did not impair fertility

exposure at use recommendation of the pharmacology 13.2 Animal Toxicology and/or Pharmacology in animal manual mature mature at every dose-level

repeat-dose studies in rats, treatment-related neutropenia occurred at every dose-re sted, including the lowest dose of 2 mg/kg (approximately 2% of the human dose on a b riface area basis).

Studiac in robbits and Dharur monhave wara inconclusive with record to the affect on

Employed in a randomized, double-blind, non-inferior drawing trial. This trial compared entapeneen (1 g infravenously once a day) with piperscillin/tacobactam (3.375 g intravenously every 6 hours) for 5 to 14 days and enrolled 665 patients with localized compilated appendicities, and any

other complicated intra-abdominal infection including colonic, small intestinal, and biliary infections and generalized peritonitis. The combined clinical and microbiologic success rates

in the microbiologically evaluable population at 4 to 6 weeks posttherapy (test-of-cure) were 83.6% (163/195) for entapenem and 80.4% (152/189) for ciceracillin/fazobactam.

Assumements. Name and a start and the present start of complicated skin and skin structure infections in a randomized, outbuel-bink non-inferiorly dirical triat. This triat compared exterplement () ginteractional crack and skin structure reference (1) ginteractions and control 4540 patients including patients with the structure of the structur

Ertanement was evaluated in adults for the treatment of diabetic foot infections without

Encourses an examine in adults for the transmit of shared to the effective setup of the example of the example

randomized to estagenese and 202 patients randomized to piperacial history patients child by evaluable. The clinical success rates at 10 days pottierapy were 75% (153/204) for estagenese and 70.8% (143/2020) for piperacialin/lazabactam.

Entanement was evaluated in adults for the treatment of community acquired oneumonia in Engineers was evaluated in adults for the treatment of community acquired greeumonia in a constrainted, doubtis met, met-freeding value was the state of the treatment of the state of the

Ertapenem was evaluated in adults for the treatment of complicated intra-abdo

Extension has been shown to be active assisted most isolates of the follow

Ifococcus agalactiae Ifococcus pneumoniae (peniciliin susceptible isolates only)

Gram-positive bacteria: Staphylococcus aureus (methicillin susceptible isolates only)

Hemophilus influenzae (beta-lactamase negative isolates only) Klebsiella pneumoniae

Gram-positive bacteria: Gram-positive bacteria: anidemidic (methicilin susceptible isolates only)

Cárobacter finundé Cárobacter kongenis Enterobacter Josephini Hiermophilos influenzie (Pete-Jactamase positive isolates only) Hiermophilos parifikenza Klebanisti confoco (excluding ESBL producing isolates) Monannelle moralita

12.1 Carcinonenerie Mutanenerie Impairment of Eartility

Antimicrobial Activity

Streptococcus agalactiae

Gram-negative bacteria:

Streatococcus manaenes

Moraxella catanhala

Bacteroides distasonis

Conternides thetaint Bacteroides uniformis Clastridium clastridioforme

ubacterium lentum Peptostreptococcus species

Gram-manative bacteris:

Morganella morgani Proteus vulgaris

rovidencia rettgeri rovidencia stuartii

Serratia manoespene

Anaerobic bacteria

Racteroides vulgatus Nostridium perfringe

usobacterium so

Susceptibility Testing

Impairment of Fertility

14 CLINICAL STUDIES

Diabetic Foot Infections

Community Acquired Pneumonia

Complicated Intra-Abdominal Infections

Complicated Skin and Skin Structure Infections

141 44-84

12 NONCLINICAL TOXICOLOGY

Carcinopenesis and Mutapenesis

Prevatella bixiz

Proteus mirabilis Anaerobic bacteria

		Singl	e I.V.º Do	ose Admi	nistratio	n			
lge Group	Dose	Average Plasma Concentrations (mcg/mL)							
		0.5 hr	1 hr	2 hr	4 hr	6 hr	8 hr	12 hr	24 hr
to 23 months	15 mg/kg 1	103.8	57.3	43.6	23.7	13.5	8.2	2.5	
	20 mg/kg 1	126.8	87.6	58.7	28.4		12	3.4	0.4
	40 mg/kg ⁼	199.1	144.1	95.7	58	-	20.2	7.7	0.6
to 12 years	15 mg/kg 1	113.2	63.9	42.1	21.9	12.8	7.6	3	
	20 mg/kg 1	147.6	97.6	63.2	34.5		12.3	4.9	0.5
	40 mg/kg ⁼	241.7	152.7	96.3	55.6	-	18.8	7.2	0.6
3 to 17 years	20 mg/kg 1	170.4	98.3	67.8	40.4		16	7	1.1
	1 g ⁵		110.9			24		6.2	-
	40 mo/kg ²	255	188.7	127.9	76.2	-	31	15.3	2.1

fused at a constant rate over 30 minute

¹ up to a maximum dose of 1 g/day ² up to a maximum dose of 2 g/day

⁴ up to a maximum dose of 2 grapy ⁵ Based on three patients receiving 1 g ertapenem who volunteered for pharmacokinetic assessment in one of the two safety and efficacy trials

Absorption Enternanter reconstituted with 1% lidocaine HCI injection, USP (in saline without epinephrine), is Ertapenern, reconstituted with 1% lidecame HCI injection, USP (in salme without geneph almost completely absorbed following intramuscular (LM) administration at the recomm dose of 1 g. The mean bioavailability is approximately 90%. Following 1 g daily LM adminis mean peak plasma concentrations (C__) are achieved in approximately 2.3 hours (T__).

earching the second to burn an electric contains, primarily alburnin. In healthy young adults the cadeterin 6 migling boots of name present proteins, primarily administrations, from approximately 95% postein binding of ertapener of decreases as prisonra concentrations increase, from approximately 95% bound at an approximate plasma concentration of < 100 micrograms (mcg)/mL to approximate) 85% bound at an approximate plasma concentration of 300 mco/mL.

The apparent volume of distribution at steady state (U) of entipement in adults is approximately 0.12 liter/kg, approximately 0.2 liter/kg in pediatric patients 3 months to 12 years of age and approximately 0.16 liter/kg in pediatric patients 13 to 17 years of age. The concentrations of entipement adultered in succlos-induced skin blister fluid at each sampling point on the third day of 1 g once daily LV does are presented in Table 10. The ratio of AUC... in skin blister fluid/AUC... in plasma is 0.61.

Table 10 Concentrations (mcg/mL) of Ertapenem in Adult Sún Blister Fluid at each Sampling Point on the Third Day of 1-g Once Daily LV. Doses 24 hr

	12	17	24	24	21	8
Metabolism						
	ing adults, afte	r infusion of 1	n I V radiolat	beled ectaneo	em the plasm	a radioactivity
consists pred	ominantly (94	%) of entaneo	em The main	r matsholita	farbanam	ir the inartice

Binimation Ertoperen is eliminated primarily by the kidneys. The mean plasma half-life in healthry young adults is approximately 4 hours and the plasma clearance is approximately 1.8 L (hour. The mean plasma half-life in prediative patients 13 to 11 years of age is approximately 4 hours and approximately 2.5 hours in prediative plasmets a month to 12 years of age.

Following the administration of 1 g.U. radiolabeled etapenem to healthy young adults, approximately 80% is recovered in unine and 10% in feces. 01 the 80% recovered in unine, approximately 30% is exercted as unchanged drug and approximately 37% as the ring-opened metabolite.

behavior as intermediated and an opportunitation of the and the may opportunitation of the administered dose excreted in unine was 17.4% during 0 to 2 hours postdose, 5.4% during 4 to 6 hours postdose, and 2.4% during 12 to 24 hours postdose.

Special Populations

Total and unbound fractions of ertapenem pharmacokinetics were investigated in 26 adult subjects (31 to 80 years of age) with varying degrees of renal impairment.

Alters (1) is to year if any with any dynamic dynamic drine laparent. The second se Henstic Impairment

The pharmacokinetics of ertapenem in patients with hepatic impairment have not been The plantiaccontenses of encipient and patients was repeated impaintent name not over established. However, estaphenem does not appear to undergo hepatic metabolism based on in who studies and approximately 10% of an administered does is recovered in the feces (see Chicael Plantamacology (72.3) and Doesawe and Administration (2.6).

The effect of gender on the pharmacokinetics of ertapenern was evaluated in healthy male (n=8 and healthy female (n=8) subjects. The differences observed could be attributed to body size when body weight was taken into consideration. No done adjustment is recommended based on gender

Geriatric Patients The impact of age on the pharmacokinetics of entanenem was evaluated in healthy male (n=7

The impact of age of the pharmacounters of endpendin was realized in the any finate (im/) and healthy freed (im/) subjects > 65 years of age. The total and unbound AUC Increases 37% and 67%, respectively, in olderly adults relative to young adults. These changes were attributed to age-related changes in creatinine clearance. No dosage adjustment is necessary for elderly patients with normal (for their age) renal function.

Darlistric Datiente

entrations of ertapenem are comparable in pediatric patients 13 to 17 years of app and adults following a 1 g once daily I.V. dose Following the 20 mg/kg dose (up to a maximum dose of 1 g), the pharmacokinetic parame in patients 13 to 17 years of age (N=6) were generally comparable to those in healthy you

Plasma concentrations at the midpoint of the dosing interval following a single 15 mg/kg LV, dose of entapenem in patients 3 months to 12 years of age are comparable to plasma doze of estiganemi in galients 3 months to 12 years of age are Compatible to plaima concentrations at the implant of the obsamp interval following a 1 g one daily 10 yeas in stalls (pe clinical Pharmacology (7.23)). The plasma clinaratic (mL minika) of estiganemi stalls (pe clinical Pharmacology (7.23)). The plasma clinaratic (mL minika) of estiganemi stalls. At he 15 mg/des. He ALC value (stalls) the clinical stall stalls) and stalls. At he 15 mg/des. He ALC value (stalls) the clinical stalls) and stalls. At he 15 mg/des. He ALC value (stalls) the clinical stalls) and stalls. At he 15 mg/des. He ALC value (stalls) the clinical stalls) and stalls. At he 15 mg/des. He ALC value (stalls) and the ALC value (stalls) and stalls in young health value (stalls) and (1 y L doze of estigation). Drug Interactions

ertapenem is co-administered with probenecid (500 mg p.o. every 6 hours), probenecid eless for active tubular secretion and reduces the renal clearance of ertapenem. Based compromision acure tubular secretion and reduces the renal clearance of extiplement. Based on total extipenent concentrations, probeneoid increased the AUC of extipenent by 20%, and reduced the plasma and renal clearance of estipanent by 20% and 35%, respectively. The half-life of ertapenent was increased from 4 to 4.8 hours.

In vitro studies in human liver microsomes indicate that entropenem does not inhibit metabolism mediated by any of the following cytochrome p450 (CYP) isoforms: 1A2, 2C9, 2C19, 2D6, 2E1 and 3A4 In witho studies indicate that entapenem does not inhibit P-glycoprotein-mediated transport of digaxin or virblastine and that entapenem is not a substrate for P-glycoprotein-mediated transport.

Enclanation consoling Enclanation of the second bacteria. The bactericidal activity of entraperent results from the inhibition of cell well synthesis and is mediated through entraperent binding to pencillin binding proteins (PBPs). In Exclericida coli, it has storing affinity baward PBPs 1a, 1b, 2, 3, 4 and 5 with preference for PBPs 2 and 3.

12.4 Microbiology Mechanism of Action